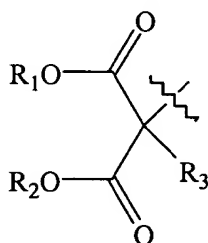


(I),

wherein:

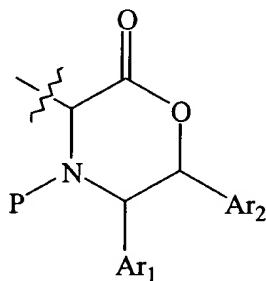
A is carboxyl, carboxyalkyl, dicarboxyalkyl, alkoxy carbonyl, alkoxy carbonylalkyl, dialkoxy carbonylalkyl, or a malonyl group of formula II:



(II),

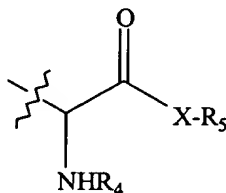
wherein  $R_1$  and  $R_2$  may be the same or different and are selected from the group consisting of hydrogen, alkyl, aryl, arylalkyl, alkylaryl, and heteroaryl; and  $R_3$  is selected from the group consisting of hydrogen, halo, hydroxy, amino, alkyl, aryl, and alkoxy;

B has the formula III:



(III),

wherein P is an amine protecting group; and  $Ar_1$  and  $Ar_2$  are aryl groups; or the formula IV:



(IV),

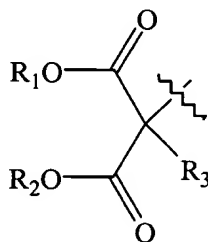
wherein X is NH or O; R<sub>4</sub> is hydrogen, alkyl, aryl, alkylaryl, arylalkyl, or an amine protective group; and R<sub>5</sub> is selected from the group consisting of hydrogen, alkyl, aryl, arylalkyl, alkylaryl, and heteroaryl; and

C is selected from the group consisting of hydrogen, hydroxyl, alkyl, alkylcarbonyl, alkylcarbonyloxy, alkoxycarbonyl, and alkoxycarbonyl alkyl;

wherein said aryl, heteroaryl, and the aryl portion of said arylalkyl and alkylaryl may be unsubstituted or substituted with a substituent selected from the group consisting of alkyl, hydroxy, halo, keto, amino, and alkoxy; with the provisos that (i) R<sub>5</sub> is not hydrogen when A is carboxyl or carboxyalkyl, C is hydrogen, B has the formula IV wherein R<sub>4</sub> is hydrogen or alkylcarbonyl, and X is NH; and (ii) R<sub>5</sub> is not hydrogen or alkyl when A is carboxyl or carboxyalkyl, C is hydrogen or hydroxy, B has the formula IV wherein R<sub>4</sub> is hydrogen or alkylcarbonyl, and X is O.

2. (Amended) The compound of claim 1, wherein:

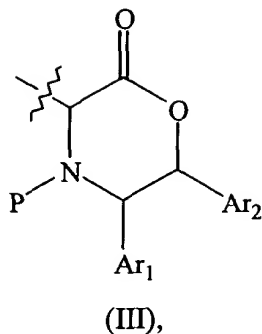
A is carboxyl, carboxyl C<sub>1</sub>-C<sub>6</sub> alkyl, dicarboxy C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub> alkoxycarbonyl C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> dialkoxycarbonyl C<sub>1</sub>-C<sub>6</sub> alkyl, or a malonyl group of formula II:



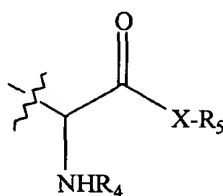
(II),

wherein R<sub>1</sub> and R<sub>2</sub> may be the same or different and are selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, aryl C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkylaryl, and heteroaryl; and R<sub>3</sub> is selected from the group consisting of hydrogen, halo, hydroxy, amino, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, and C<sub>1</sub>-C<sub>6</sub> alkoxy;

B has the formula III:



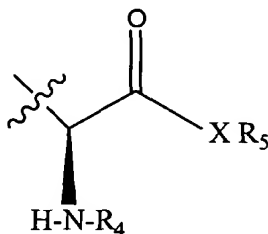
A<sup>2</sup> wherein P is an amine protecting group; and Ar<sub>1</sub> and Ar<sub>2</sub> are aryl groups; or B has the formula IV:



wherein X is NH or O; R<sub>4</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, C<sub>1</sub>-C<sub>6</sub> alkylaryl, aryl C<sub>1</sub>-C<sub>6</sub> alkyl, or an amine protecting group; and R<sub>5</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, aryl C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkylaryl, and heteroaryl; and

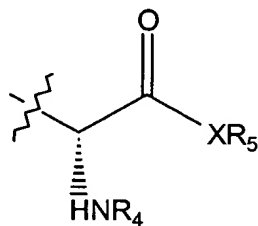
C is selected from the group consisting of hydrogen, hydroxyl, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkylcarbonyl, C<sub>1</sub>-C<sub>6</sub> alkylcarbonyloxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, and C<sub>1</sub>-C<sub>6</sub> alkoxy C<sub>1</sub>-C<sub>6</sub> alkyl; wherein said aryl, heteroaryl, and the aryl portion of said arylalkyl and alkylaryl may be unsubstituted or substituted with a substituent selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy, halo, keto, amino, and C<sub>1</sub>-C<sub>6</sub> alkoxy.

4. (Amended) The compound of claim 3, wherein B has the formula:



wherein X is NH or O; R<sub>4</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, C<sub>1</sub>-C<sub>6</sub> alkylaryl, aryl C<sub>1</sub>-C<sub>6</sub> alkyl, or an amine protecting group; and R<sub>5</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, aryl C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkylaryl, and heteroaryl.

5. (Amended) The compound of claim 3, wherein B has the formula:



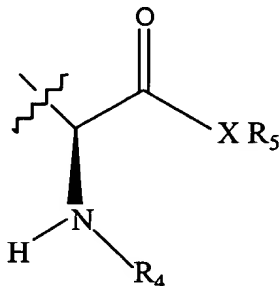
wherein X is NH or O; R<sub>4</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, C<sub>1</sub>-C<sub>6</sub> alkylaryl, aryl C<sub>1</sub>-C<sub>6</sub> alkyl, or an amine protecting group; and R<sub>5</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, aryl C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkylaryl, and heteroaryl.

6. (Amended) The compound of claim 4, wherein X is O.

A<sup>4</sup>

9. (Amended) The compound of claim 8, wherein the amine protecting group is selected from the group consisting of fluorenylmethoxycarbonyl, tert-butoxycarbonyl, carbobenzoxy, and carbamoyl.

24. (Amended) The compound of claim 1, wherein R<sub>1</sub> and R<sub>2</sub> are tert-butyl, R<sub>3</sub> is hydrogen, and B has the formula



wherein X is O, R<sub>4</sub> is fluorenylmethoxycarbonyl, and R<sub>5</sub> is hydrogen.

A6

34. (Amended) A conjugate comprising a conjugant covalently linked to a compound of claim 1.

A7

44. (Amended) The compound of claim 41, wherein E is hydrogen.

A8

46. (Amended) The compound of claim 41, wherein R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, and R<sub>6</sub> are hydrogen.

A9

48. (Amended) The compound of claim 38, wherein W is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkylcarbonyl, oxalyl, C<sub>1</sub>-C<sub>6</sub> alkylaminooxalyl, arylaminooxalyl, aryl C<sub>1</sub>-C<sub>6</sub> alkylaminooxalyl, C<sub>1</sub>-C<sub>6</sub> alkoxyoxalyl, carboxy C<sub>1</sub>-C<sub>6</sub> alkyl carbonyl, heterocyclyl carbonyl, heterocyclyl C<sub>1</sub>-C<sub>6</sub> alkyl carbonyl, aryl C<sub>1</sub>-C<sub>6</sub> alkyl heterocyclyl C<sub>1</sub>-C<sub>6</sub> alkyl carbonyl, aryloxy carbonyl, and aryl C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, wherein the aryl and alkyl portions of the substituents may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino, amino C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, and keto; and the heterocyclyl portion of W contains at least 4 hetero atoms selected from the group consisting of O, N, and S.

A10

66. (Amended) The compound of claim 38, wherein Z is aryl C<sub>1</sub>-C<sub>6</sub> alkylamino.

A11

71. (Amended) The compound of claim 38, wherein Z is aryl heterocyclyl C<sub>1</sub>-C<sub>6</sub> alkylamino.

A12

77. (Amended) The compound of claim 38, wherein said amino acid is selected from the group consisting of glycine, alanine, valine, norvaline, leucine, iso-leucine, norleucine,  $\alpha$ -amino n-decanoic acid, serine, homoserine, threonine, methionine, cysteine, S-acetylaminomethyl-cysteine, proline, trans-3- and trans-4-hydroxyproline, phenylalanine, tyrosine, 4-aminophenylalanine, 4-nitrophenylalanine, 4-chlorophenylalanine, 4-carboxyphenylalanine,  $\beta$ -phenylserine  $\beta$ -hydroxyphenylalanine, phenylglycine,  $\alpha$ -naphthylalanine, cyclohexylalanine, cyclohexylglycine, tryptophan, indoline-2-carboxylic acid, 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, aspartic acid, asparagine, aminomalonic acid, aminomalonic acid monoamide, glutamic acid, glutamine, histidine, arginine, lysine, N'-benzyl-N'-methyl-lysine, N',N'-dibenzyl-lysine, 6-hydroxylysine, ornithine,  $\alpha$ -aminocyclopentane carboxylic acid,  $\alpha$ -aminocyclohexane carboxylic acid,  $\alpha$ -aminocycloheptane carboxylic acid,  $\alpha$ -(2-amino-2-norbornane)-carboxylic acid,  $\alpha,\gamma$ -

A<sup>12</sup>  
diaminobutyric acid,  $\alpha,\beta$ -diaminopropionic acid, homophenylalanine, and  $\alpha$ -tert-butylglycine.

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A<sup>13</sup>  
84. (Amended) A composition comprising a pharmacologically acceptable carrier and a compound of claim 38.

85. (Amended) A method for inhibiting an SH2 domain from binding with a phosphoprotein comprising contacting an SH2 domain with a compound of claim 38.

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90. (Amended) A method for inhibiting SH2 domain binding comprising exposing a material containing an SH2 domain to a compound of claim 38.

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A<sup>14</sup>  
91. (Amended) A method for determining the presence of an SH2 domain in a material comprising:

(a) exposing a sample of said material to a SH2 binding compound and obtaining a first binding result;

(b) exposing another sample of said material to a compound of claim 38 and obtaining a second binding result; and

(c) comparing the first and second binding results to determine whether an SH2 domain is present in the material.

92. (Amended) A method of preventing or treating a disease, state, or condition in a mammal comprising administering a compound of claim 38.

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A<sup>15</sup>  
106. (Amended) A method of enhancing the therapeutic effect of a treatment rendered to a mammal that has been afflicted with a disease, state, or condition, comprising administering to the mammal a compound of claim 38 in conjunction with the treatment.

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A<sup>16</sup>  
112. (Amended) A method of inhibiting the MAP kinase activity in a mammal comprising administering to the mammal a compound of claim 38.

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Add the following claims:

R-126  
116  
115. (New) A compound of the formula:

W-Y-(AA)<sub>n</sub>-Z

A<sup>17</sup>  
wherein n is 0 to 15;

Y is a phenylalanyl radical having a phenyl ring, an amine end, and a carboxyl end, the phenyl ring having (i) dicarboxy C<sub>1</sub>-C<sub>6</sub> alkyl, (ii) hydroxyl and carboxy C<sub>1</sub>-C<sub>6</sub> alkyl, (iii) carboxyl and carboxy C<sub>1</sub>-C<sub>6</sub> alkyl, or (iv) dicarboxyhalo C<sub>1</sub>-C<sub>6</sub> alkyl, or dicarboxyhalo C<sub>1</sub>-C<sub>6</sub> alkyloxy; or an ester of (i), (ii), (iii), or (iv); wherein the alkyl portion of the substituents may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino, aminoalkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, and keto;

W is a moiety attached to the nitrogen of Y and is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkylcarbonyl, oxalyl, C<sub>1</sub>-C<sub>6</sub> alkylaminooxalyl, arylaminooxalyl, aryl C<sub>1</sub>-C<sub>6</sub> alkylaminooxalyl, C<sub>1</sub>-C<sub>6</sub> alkoxyoxalyl, carboxy C<sub>1</sub>-C<sub>6</sub> alkyl carbonyl, heterocyclyl carbonyl, heterocyclyl C<sub>1</sub>-C<sub>6</sub> alkyl carbonyl, aryl C<sub>1</sub>-C<sub>6</sub> alkyl heterocyclyl C<sub>1</sub>-C<sub>6</sub> alkyl carbonyl, aryloxy carbonyl, and aryl C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, wherein the aryl and alkyl portions of the substituents may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino, amino C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, and keto; and the heterocyclyl portion of W contains at least 4 hetero atoms selected from the group consisting of O, N, and S;

AA is an amino acid, the amine end of which is attached to the carboxyl end of Y; and

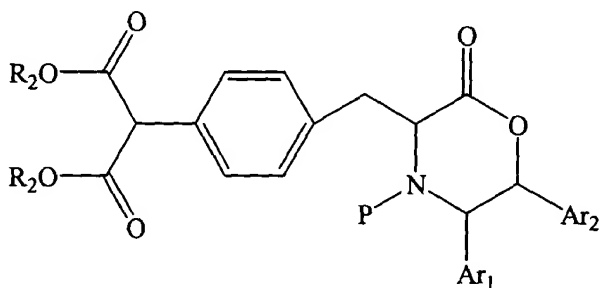
Z is an aryl C<sub>1</sub>-C<sub>6</sub> alkylamino or arylheterocyclyl C<sub>1</sub>-C<sub>6</sub> alkylamino;

or a salt thereof.

117  
116. (New) A composition comprising a pharmacologically acceptable carrier and a compound of claim 115.

118  
117. (New) A method for inhibiting an SH2 domain from binding with a phosphoprotein comprising contacting an SH2 domain with a compound of claim 115.

119  
118. (New) A process for the preparation of a compound of formula VII:



(VII),

wherein  $R_2$  is alkyl, P is an amine protecting group, and  $Ar_1$  and  $Ar_2$  are aryl; the process comprising:

- A17
- (a) converting a p-halotoluene to a p-tolyl-malonic acid dialkyl ester by contacting the p-halotoluene with a dialkylmalonate and a cuprous halide;
  - (b) halogenating the p-tolyl-malonic acid dialkyl ester to obtain a (4-halomethylphenyl)-malonic acid dialkyl ester; and
  - (c) contacting the (4-halomethylphenyl)-malonic acid ester with a benzyl-6-oxo-2,3-diaryl-4-morpholine to obtain the compound of formula VII.
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